Efficacy of Dihydroergocristine 20mg Once Daily in Patients with Organic Brain Psychosyndrome
A 3-Month Randomised, Double-Blind, Placebo-Controlled Study

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Summary

Forty outpatients (20 men and 20 women) aged 60 to 80 years (mean age 69.9 ± 5.5 years) with a diagnosis of organic brain psychosyndrome took part in a 3-month randomised, double-blind study aimed at comparing the effectiveness and safety of dihydroergocristine 20mg once daily and placebo. The patients had experienced memory impairment and reduced concentration and clarity of thought, and/or personality and affective disorders for at least 6 months. Patients had a Hachinski Dementia Score ≤15, a Hachinski Ischemic Score <5, and a Hamilton Rating Scale for Depression score of ≤22. The Sandoz Clinical Assessment-Geriatric (SCAG) scale, used as the efficacy variable, was administered on study entry and during (45 days) and after (90 days) treatment. Safety evaluations (routine laboratory tests and measurements of systolic and diastolic blood pressure and heart rate) were performed before and at the end of the study period. All patients fulfilled the entry criteria and completed the study protocol. In the dihydroergocristine group, there was a marked improvement in the SCAG total score and in most partial scores compared with baseline values. Most symptoms had already improved significantly after 45 days of treatment with dihydroergocristine.

In the placebo group, no clinically relevant or statistically significant changes in SCAG scores relative to baseline values were seen at the end of the study period. Safety was assessed as very good in all patients. No adverse events were reported, except for one case of mild self-limiting nausea during dihydroergocristine treatment. No clinically relevant or statistically significant changes relative to baseline values were found in laboratory parameters or in blood pressure and heart rate measurements performed at the end of each treatment. The results of this study suggest that dihydroergocristine 20mg once daily is effective and safe in the treatment of organic brain psychosyndrome.
Brain ageing is a complex process characterised by progressive changes in the morphological and functional structure of the central nervous system (CNS). These changes include neuronal loss, decreased synthesis of neurotransmitters and/or decreased responsiveness of receptors, with a marked impairment in cellular metabolism.

In physiological conditions, compensatory processes counteract these changes and are generally sufficient to guarantee satisfactory homeostasis. However, a percentage of the elderly population shows a decrease in mental alertness, an impairment in short term memory and selfcare, and symptoms of affective disorders, without signs of cerebrovascular disease or other chronic brain syndromes. Circulatory insufficiency in some cerebral regions, caused by vascular failure of arteriosclerotic origin or by cerebrovascular accidents, represents a frequent pathology in the elderly population.

As is well documented, dihydroergocristine, an ergot alkaloid obtained by hydrogenating the lysergic acid moiety of ergocristine, is a compound that has pharmacological activity at α-adrenergic, serotonergic and dopaminergic receptors, with interesting effects on cerebral metabolism.

Pharmacokinetic studies after oral administration of dihydroergocristine in humans showed a kinetic profile resembling that of other ergot alkaloids, with a long elimination half-life and a large volume of distribution; the absolute oral bioavailability of the compound ranged between 4.6 and 6.1%.

Dihydroergocristine at a dosage of 6 mg/day has been used successfully in the management of elderly patients with organic brain psychosyndrome with or without cerebrovascular disease, and the incidence of adverse events observed in long term studies of the drug can be considered very low.

In previous pharmacodynamic studies, dihydroergocristine doses of 20 and 40 mg/day have been used for 3 to 9 months without an increase in the frequency of adverse events. Thus, the aim of the present clinical trial was to evaluate the efficacy and safety of dihydroergocristine 20 mg/day in patients with organic brain psychosyndrome.

Patients and Methods

Patients

Forty outpatients (20 men and 20 women), aged 60 to 80 years (mean age 69.9 ± 5.5 years), with a diagnosis of organic brain psychosyndrome were included in the study provided that their witnessed informed oral consent had been obtained.

Inclusion and Exclusion Criteria

The following inclusion criteria were applied: impairment of cognitive function to the extent that normal social and working activities were impaired; impairment of memory; presence of at least one of the following — reduction of concentration and clarity of thought, personality disorder, affective disorder, deterioration in selfcare; and a Hamilton Rating Scale for Depression score of ≤22, a Hachinski Dementia Score of ≤15 and a Hachinski Ischemic Score <5.

All symptoms had to have been present for at least 6 months and had to have shown a progressive worsening.

Patients with symptoms of multi-infarct dementia, Parkinson’s disease, Huntington’s disease, multiple sclerosis, epilepsy, psychiatric diseases, and toxic or metabolic cerebral disorders were excluded, as were patients with uncompensated diabetes and those with clinically relevant gastrointestinal, hepatic, renal, cardiovascular or respiratory disorders.

Methods

Patients had to discontinue any therapy with other CNS-active drugs 15 days before starting the study. During the treatment period, they were only allowed to take benzodiazepines if needed.

The patients were randomly allocated to two groups of 20 patients each, and each group received either dihydroergocristine 20mg or an indistinguishable placebo once daily for 3 months.

The Sandoz Clinical Assessment-Geriatric (SCAG) scale was used to evaluate the efficacy